THE USE OF ELECTRIC MUSCLE STIMULATION TO ENHANCE BOTULINUM TOXIN ACTION IN SPASTIC STROKE PATIENTS

Thesis
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Chapter I

Introduction

Stroke is the clinical term for acute loss of perfusion to vascular territory of the brain, resulting in ischemia and a corresponding loss of neurologic function. Stroke was classified as either hemorrhagic or ischemic, typically manifest with the sudden onset of focal neurologic deficits, such as weakness, sensory deficit, or difficulties with language. Ischemic strokes have a heterogeneous group of causes, including thrombosis, embolism, and hypoperfusion, whereas hemorrhagic strokes can be either intraparenchymal or subarachnoid **(Edward, 2007).**

Post-stroke hemiparesis, together with abnormal muscle tone, are major causes of morbidity and disability. Although most hemiparetic patients are able to reach different ambulatory levels with rehabilitation efforts, upper and lower limb spasticity can impede activities of daily living, personal hygiene, ambulation and, in some cases, functional improvement **(Suheda and Koncuy, 2007).**

Spasticity is a motor disorder characterized by a velocity dependant increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerk resulting from hyperexcitability of the stretch reflex. Spasticity is one component of the upper motor neuron syndrome **(Katz and Rymer, 1989).** Spasticity of the planterflexors is the most important independent determinant of temporal and spatial gait asymmetry during comfortable speed and fast speed walking **(Tang and Jan, 2003).**

Spasticity of distal lower limb muscle groups such as the ankle plantarflexors causes reduced ambulatory speed, gait dysfunction and increased risk of falls. Gait asymmetry is influenced primarily by the degree of spasticity of the planterflexors **(Lamon et al., 2001).**

Impaired walking is one of the main functional problems that the physiotherapist encounter in caring for neurologically impaired patient. Range of motion (ROM), posture, bony alignment, muscle power, motor control, coordination, sensation and balance are the factors which could affect the ability to walk **(Janet and Roberta, 2003).**

The ability to walk independently is a pre request for most activities of daily living. It has been reported that only 70 % of the patients discharged from rehabilitation met the criteria for community walking, which include the ability to walk 500 meters continuously at a speed that would enable them to cross a road safely **(Hill and Ellis, 1997).** Gait dysfunction persists in individuals with stroke, although approximately 65–85% of patients are able to walk independently by six months following a stroke **(Sujin et al., 2010).**

Spasticity can lead to significant physical problems including spasms, restricted range of movement, pain, and contractures, as well as functional difficulties including the maintenance of personal hygiene. The treatment with Botulinum toxin seemed safe with the potential both to reduce spasticity and improve function, Botulinum toxin is now used clinically for a wide range of conditions, particularly focal dystonias, and increasingly for spasticity **(Elizabth and Michael., 2000).** Electrical stimulation may enhance the effectiveness of botulinum toxin A in patients with chronic upper-limb spasticity **(Christine et al., 2006).**

Nerve stimulation of various stimulation frequencies used to enhance the absorption rate of Botulinum toxin. Nerve stimulation of the muscle injected with botulinum toxin delay sprouting **(Emma et Al., 2005).** Reports suggest that protocols of low frequency electrical stimulation of injected muscles after injection enhance the blocking effect of Botulinum toxin **(Simpson et al., 2008).**

Statement of the problem:

Whether there is a significant effect of electric muscle stimulation enhance botulinum toxin action and can effectively control ankle plantar flexors spasticity and provides functional improvement of gait in spastic stroke patients?

Purpose of the study:

Was to investegate the effect of electric muscle stimulation on enhancing botulinum toxin action in treating spastic stroke patients and improve gait.

Significance of the study:

Spasticity is a common complication of stroke patients, particularly in ankle planter flexion and inversion, that causing problems like impaired foot contact, dragging of toes, reduced stance duration and stride length **(Suheda and Koncuy, 2007).**

Emma et al.,(2005) questioned whether muscle activity induced by electrical muscle or nerve stimulation effectively increases the effect of Botulinum toxin in spastic muscle. Conclusion was that nerve stimulation enhances the effect of Botulinum toxin induced denervation by facilitating the lytic step that blocks acetylcholine transmission at neuromuscular junction.

Hypothesis:

It was hypothesized that electric muscle stimulation could not enhance botulinum toxin action in controlling planterflexors spasticity and improve gait in spastic stroke patients.

Basic assumptions:

It was assumed that:

• The patients were received the same physical therapy program and botulinum toxin injection therapy.

• The caliberations of the equipments used in this study were accurate.

• The patient's motivation and cooperation were the same for each one.

• The patients were exert the maxmimum effort during assessment and treatment.

• All other factors which may influence the outcome such as noise, distraction … etc, were controlled.

• The results obtained from this study were of value in physical therapy field.

Limitations:

An effort were made to minimize the effect of possible errors. The possible limitation may be as following:

• Personal coopration level of the patients.

• Psychological status of the patients may affect the treatment records.

Delimitations:

This study was delimited to the following:

1- Forty stroke patients of both sexs were included in this study.

2- Patients age ranged from 45 to 55 years.

3- Patients were referred from a neurologist as cerebrovascular stroke patients.

4- The duration of stroke ranged from six to eighteen months.

5- Patients were free from any orthopeadic changes (such as muscle shortening, contractures, joint stiffness…etc).

6- The patients were able to walk independantly.

7- The degree of ankl planterflexors spasticity ranged from grade two to three according to modified Ashworth scale **(Bohannon and Smith, 1987; Emma et al., 2005) .**

8- The patients were free from cognitive or perceptual impairments.

9- The patients were free of other neurological disorders.

Definition of terms:

- Botulinum toxin:

Is a neurotoxin produced by the anaerobic bacterium, Clostridium botulinum. When injected intramuscularly, it prevents the release of acetylcholine from presynaptic vesicles at the neuromuscular junctions resulting in temporary, reversible block of the motor fibers and weakened muscle contraction ***(Simpson, 2000).***

- Spasticity:

Spasticity is a motor disorder characterized by a velocity dependant increase in tonic stretch reflex (muscle tone) with exaggerated tendon jerk. It is one of the components of the upper motor neuron syndrome. It results from hyperexcitability of the stretch reflex **(Katz and Rymer, 1989).**

-3-D measurements:

It is the detection of the trajectories of several points that identify the position of body segments in space. Involves a sophisticated computerized video cameras that automatically digitizes the position of each point in space to provide a 3-D position of the body segment **(Allar et al., 1995).**

Chapter II

LITERATURE REVIEW

Chapter II

LITERATURE REVIEW

This chapter discussed the following items:

- Stroke.

Stroke risk factors.

Stroke classification.

Stroke pathology.

Stroke signs and symptoms.

Stroke recovery.

- Spasticity.

Physiology of muscle tone.

Pathophysiology of spasticity.

Quantification of spasticity.

Assessment of spasticity.

- Gait.

Normal gait

Gait analysis.

Characteristics of hemiplegic gait.

- Botulimum toxin.

Background information.

Botulinum toxin Structure.

Botulinum toxin Mechanism of Action.

Botulinum Toxin Commercial Preparations.

Botulinum toxin Intoxication Symptoms.

Types of botulism.

Effect of Botulinum Toxin Injection.

Adjunctives to improve efficacy of Botulinum Toxin Injection.

Safety of Botulinum Toxin Injection.

Botulinum Toxin Benift-risk evaluation.

Advers effect of Botulinum Toxin Injection.

Uses of Botulinum Toxin Injection.

- Electric stimulation.

Different electrical stimulation techniques in stroke.

Electric stimulation and spasticity.

Effect of electric muscle stimulation in enhancing botulinum toxin effect.

Stroke

Stroke has been defined as a sudden onset of focal and global neurological symptoms due to diseases of cerebral blood vessels leading to hemorrhage and ischemia in the brain ***(Sacco et al., 1995)***. Stroke has social and economic implications. For this reason, determination of the etiology of the disease and, especially, eradication of the risk factors is of great importance ***(Zeynep et al., 2010).***

World-wide, stroke is a common and devastating event, which often results in death or major loss of independence with immense human and financial costs. The majority of strokes are not fatal, and the major burden is long-term disability (***Martin and Elliot, 1998; Abdishakur et al., 2010).***

Stroke most commonly occurs in late middle and old age. Stroke usually occurs in patients with risk factors including hypertension, atrial fibrillation, smoking and diabetes mellitus ***(Warlow et al., 1996).***

Stroke risk factors:

Hypertension is a major factor in the development of thorombotic cerebral infarction and intracerebral haemorrhage. Cardiac disease (i.e. cardiac enlargement, failure, arrhythmias….etc) is a risk factor. Diabetes; the risk increased two folds in diabetes mellitus. Heredity; close relatives are at only slight greater risk than non-genetically related family members. Blood lipids, cholesterol, smoking, diet/obesity, these factors are much less significant than genesis of coronary heart disease ***(Kenneth et al., 2004)***.

Stroke Classification:

Stroke was classified according to the site of the lesion into: Middle cerebral artery occlusion which causes contralateral hemiplegia, hemianesthesia, hemianopia, apraxia, and aphasia if lesion is in the dominant hemisphere. Internal carotid artery occlusion plus the ocular symptoms. Anterior cerebral artery occlusion produces contralateral hemiplegia, appearance of grasp reflex and urinary incontinence. Posterior cerebral artery occlusion leads to contralateral hemisensory loss, thalamic pain, and alexia if lesion is in the dominant hemisphere. Vertebrobasilar artery occlusion produces contralateral body weaknees, sensory abnormalities, ophthalmoplegia, pupillary abnormalities, tetraparesis, semiconsciousness, pseudobulbar palsy and death often results ***(fig. 1 a, b, c)(Caronna, 2003)).***

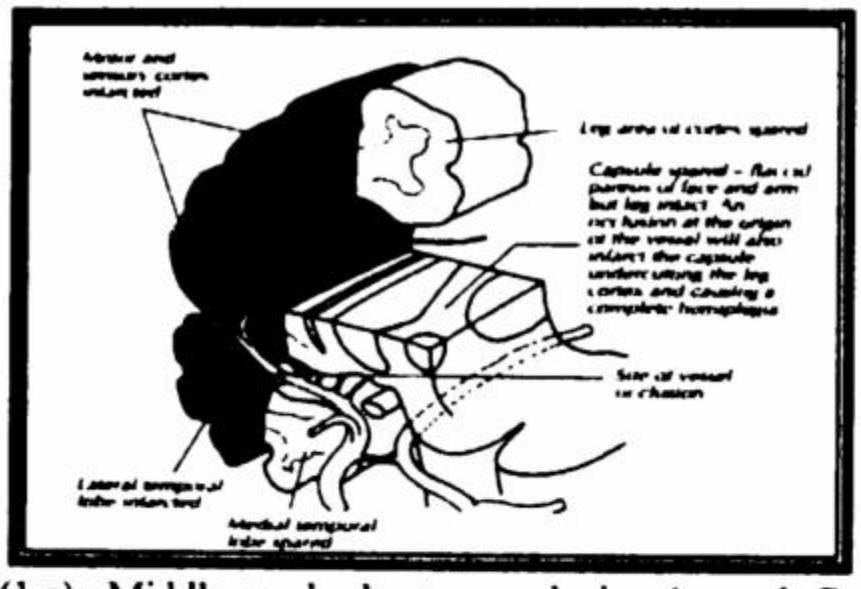

fig. (1,a): Middle cerebral artery occlusion (coated: Caronna, 2003).

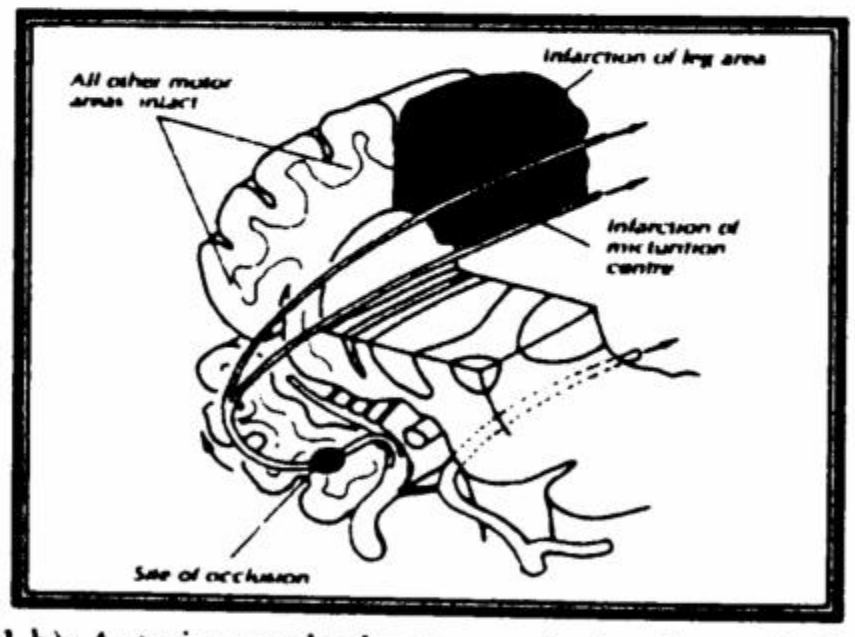

fig. (1,b): Anterior cerebral artery occlusion (coated: Caronna, 2003).

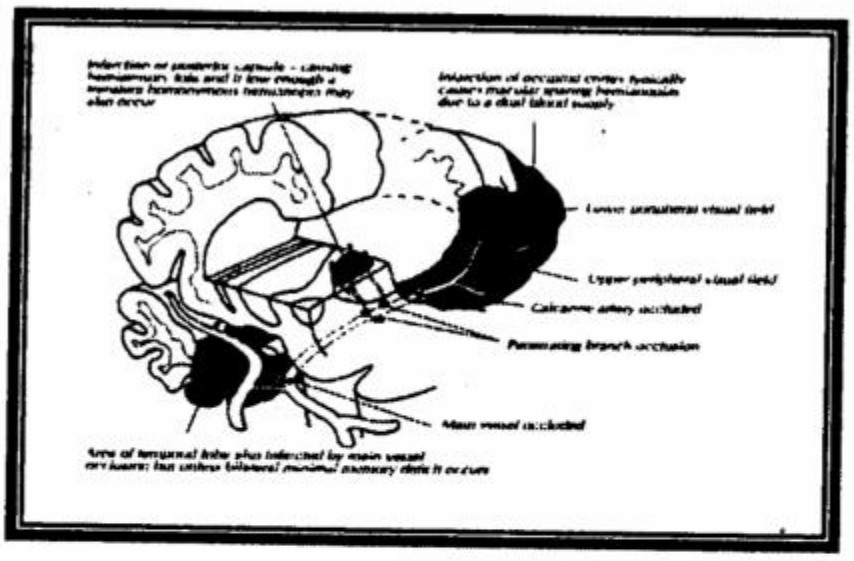

Fig. (1,c): Posterior cerebral artery occlusion (coated: Caronna, 2003).

Stroke Pathology:

Distal to occlusion of a large artery, there is a fall in the cerebral perfusion pressure (CPP) that leads to a series of haemodynamic and metabolic changes of increasing severity depending on the extent and duration of occlusion. There is an autoregulatory stage of haemodynamic reserve in which vasodilatation causes an increase in cerebral blood volume (CBV). Disturbance of this mechanism causes ischemic neural damage ***(Barork et al., 1981).*** Atherosclerosis, which produces plaque formation and progressive narrowing of the vessels and cerebral thrombosis, is a major contributory factor in occlusive vascular disease ***(Sandercock and Williams, 1993).***

The main categories of stroke are; ischemic stroke 80% of cases, intracerebral haemorrhage 15% and subarachnoid haemorrhage 5%. About 50% of ischemic strokes are due to atherothromboembolism, 25% are due to intracranial small vessel disease, 20% are due to embolism from the heart and 5% are due to rare causes ***(Warlow et al., 1996).*** There is a male preponderance in the incidence of both haemorrhagic and ischaemic CVA. There is also a preponderance of ischaemic CVA over

haemorrhagic CVA. A few intracranial pathologies that mimic CVA are misdiagnosed as CVA clinically ***(Eze et al., 2009).***

Stroke Signs and symptoms:

Headache is usually severe and the onset instantaneous. A transient or prolonged loss of consciousness or epileptic seizure, nausea and vomiting. Signs of meningism developed after 3-12 hours after the onset (neck stiffness present in most of the patients). Focal damage from haemorrhage produce focal signs (i.e. limb weakness dysphasia...etc). Epilepsy frequently occurs and may mask other features. Reactive hypertension commonly develops (i.e. rise in blood pressure in patients with no evidence of pre-existing hypertension and takes several days to return to normal levels) ***(Kenneth et al., 2004).***

Stroke recovery:

There were significant changes in the motor scores for the hemiplegic upper and lower limbs over one year. Many studies have found that motor recovery is greatest in the first month following stroke. Some authors have reported changes between three and six months with more varied improvements after this time ***(Frances et al., 2009).***

It was concluded that little recovery can be expected six months or more post stroke ***(Anderew et al., 1989).*** Descriptive research documents says that African American and Latinos who have experienced an acute stroke recover more slowly than Caucasians in the United States ***(Melanie et al., 2009).***

In people who have suffered mild to moderately severe stroke at onset, muscle strength and 2-point discrimination in the paretic UE in the

first month post-stroke are the best early predictors of the recovery of dexterous hand function at 6 months ***(Stephanie et al., 2009).***

SPASTICITY

Lehmann et al., (1989) spasticity was defined as a rate dependent reflex hypertonia triggered by stretch reflexes. It is often combined with other motor deficits, produce secondary complications and interfere with function.

Physiology of Muscle tone:

Normal muscle tone reflects a balance or equilibrium between inhibitory and excitatory inputs to the αMN. An alteration of this equilibrium results in spasticity. The stretch reflex consists of an input to the αMN resulting in an output. The input pathway is relatively complex and is modulated by several excitatory and inhibitory signals. Ia spindle afferents from muscle spindle stretch receptors enter the dorsal horn of the spinal cord and synapse with the αMN in the anterior horn with the excitatory amino acids glutamate and aspartate as neurotransmitters. These afferents also synapse on the αMN of the synergist muscle to enhance contraction and on inhibitory interneurons (Ia inhibitory interneuron) to inhibit contraction of the antagonistic muscle. The sensitivity of muscle spindle afferents is maintained by gamma (γMN) that regulates fusimotor muscle spindle tone. When a muscle is stretched, fusimotor discharges increase regulating αMN activity and reflex muscle tone. The stretch reflex also includes Renshaw recurrent inhibition, non-reciprocal autogenic (Ib) inhibition and presynaptic inhibition ***(Gordon and Ghez, 1991; Young, 1994; Brown, 1994 and Mayer, 1997).***

The stretch reflex output is simple, it occurs with the generation of an action potential and release of acetylcholine at the neuromuscular junction. This induces a muscle-end plate potential with release of calcium ions from the sarcoplasmic reticulum. An energy-required to enables myosin and actin filaments to slide over one another the final outcome is myofiber contraction ***(Ghez, 1991).***

Pathophysiology of spasticity:

On the basis of the simple input and output circuitry, several spinal mechanisms for spasticity could be postulated. The excessive activity of the fusimotor system could yield a spindle that is overly sensitive to stretch ***(Davidoff, 1985)***. The excitatory interneurons are more sensitive to muscle afferent ***(Katz and Rymer, 1989).*** Spasticity could result from hyperexcitability of the agonist αMN, perhaps from a change in the membrane properties ***(Davidoff, 1992 and Young, 1994).*** However, disruptions of synaptic input to αMN are more likely than intrinsic alterations ***(Heckman, 1994).***

Quantification of spasticity:

Measurement of spasticity has always presented a problem to clinicians. Yet, there is no literature addressing the reproducibility of the existing barrage of clinical evaluations of spasticity and reflex measurement ***(Levin and Hui-Chan, 1993). Burridge et al., (2005)*** mentioned that when spasticity is measured objectively, spasticity is measured parse and this degree of spasticity obtained could be contaminated by many other variables so we have to relate spasticity to function, to see its effect on function. Moreover, ***Voerman et al., (2005)*** stated that the most common methods to measure spasticity objectively are H reflex and T reflex. Those methods are characterized by moderate reliability and sensitivity so spasticity measurement should be correlated

with other parameters (clinical, biomechanical and neurophysiological). ***Platz et al., (2005)*** mentioned that the clinical scales as Ashworth's and modified Ashworth's scales have high interrater reliability.

Assessment of Spasticity:

Evaluation and interpretation of the tone disorders are complex, controversial, and subject to many misconceptions. An important element of demonstrating the value of a certain treatment intervention is to measure its effectiveness. Evaluation may be done either by direct measurement of impairment ***(Shiavi et al., 1997)***, or by indirect measurement of functional ability ***(Harris, 2000).***

Direct measurement of spasticity:

Observation: The patient should be placed in a comfortable supine lying position and observe any abnormal pattern that suggests the process of tone abnormalities. Also any involuntary movement may be indicative of dystonia and complete absence of spontaneous activity of the subject may be indicative of hypotonia ***(O'sullivan and Schmitz, 1994).***

Passive movement: ***Ashworth (1964)*** offered a gross clinical scale assessing muscle tone on a scale of 0 (normal) to 4 (severe). Muscle tone is assessed bilaterally and separately for the upper and lower extremities **(Appendix I)**. The manual passive stretch maneuver consists of lengthening and shortening the muscle corresponding to a specific joint. Spasticity is detected by noting the degree of resistance offered by the muscles during passive movement ***(Dimitrijevic et al., 1991).***

Tendon jerk: Eliciting the reflex in a number of tendons is a common clinical and bed side test which is generally easy to administer.

It provides a clinical impression which is highly subjective and it would be essential to supply a reproducible stimulus and measure the degree of deflection ***(Burry, 1992).***

Indirect measurement of spasticity:

Spasticity affects dexterity and functional activities. There are changes in the functional ability of the patient. These changes may indicate change in the grade of spasticity. There are many available valid and reliable measurement of functional ability, but there are conflicting opinions about their validity in measuring spasticity. The functional measurements provide useful parameters of activities of daily living but did not reflect spasticity purse ***(Pederson et al., 1997).***

Fugl-Meyer Scale: is an accurate and objective method of assessing function (but not necessarily spastic hypertonia) in hemiplegic patient. It is based on the natural progression of functional return observed by previous investigators. This scale has intratester and intertester reliability, and can be completed in a period of 10 to 20 minutes **(Appendix II)** ***(Fugl Meyer et al., 1985).***

Associated reactions: defined as abnormal reflexive movement of the affected side, which would duplicate the typical stereotyped reaction that appear closely related to activity and effort on the non affected side of the patient. Both seen difficult to quantify. This would be essential if associated reaction were used in measurement of spasiticity, as in a study compared with isokinetic measurements. The authors use the goniometry to measure differences in joint position before and after a specified movement. The use of associated reaction in the measurement of spasticity appears to be of limited value ***(Dvir and Panturin, 1993).***

Pendulum Test: has been a frequently used to assess spasticity of the knee extensor muscle. In this test, the patient is instructed to lie in a supine lying position on a tilting table with both knees flexed over the edge of the table hanging both legs freely outside. He brings the leg to a horizontal position and then the limb is allowed to fall freely as the angle of the knee is recorded by an electrogoniometer which is fitted previously to the outer surface of the knee joint ***(Bajed and Bowman, 1982).***

Biomechanical investigation of spastic hypertonia:

The biomechanical investigations attempted to quantify changes in phasic and tonic reflex activity within the limb of spastic patients. Quantitative observation can be made of torque (the amount of force elicited by moving a limb over a specified angle), threshold (particular angle where torque or EMG records significant increase and EMG which is rectified signal analysis from superficial muscle groups ***(Katz and Rymer, 1989).***

Electrophysiological testing:

A wide variety of electrophysiologic reflex studies that had been performed to assess spasticity and explore neuronal circuits within the spinal cord. The M-response is a compound muscle action potential generated by maximally stimulating a peripheral nerve and recording over a muscle innervated by that nerve. The H-reflex is not a direct response of muscle to stimulation of its motor nerve, but rather a reflex similar to muscle stretch reflex ***(Eisen and Odusote, 1999).***

The H/M ratio has been used to assess the excitability of the motor nucleus by determining the percentage of motor neurons activated via the H-reflex in comparison to direct activation of the motor neurones. There is increase in H/M ratio in the spastic phase of hemiplegia and spinal cord

injuries ***(Little and Halar, 1985)***. The H-reflex studies may be influenced by changes in stimulation frequency, patient relaxation, limb position or changes in head and neck position ***(Hugon, 1993)***.

Normal Gait

Locomotion is the process by which animals move from one geographic position to another. It includes starting, stopping, changes in speed, and alteration in directions. These events are superimposed to a basic pattern that can be defined as a rhythmic displacement of body parts that maintains the animal in constant forward progression ***(Nicola et al., 2009)***.

Normal walking is a repetitive sequence of limb motion to move the body forward while simultaneously maintaining stance stability. Each complete gait cycle consists of stance and swing phases. The entire period during which the foot is on the ground is the stance phase. The swing phase begins once the foot leaves the floor, and ends when the heel is placed down. This is accompanied with clockwise and anticlockwise rotations of the trunk opposite the pelvic rotations. In addition, pelvis drops with each step few degrees on the non weight bearing leg. Simultaneously, hip abductors of the weight bearing leg contract to prevent falling on the unsupported side ***(Galley and Forster, 1987; and Jacquelin, 1992)***.

Gait cycle can be divided into eight sub phases. The sequential combination of the phases enables the limb to accomplish three basic tasks. These are weight acceptance, single limb support, and limb advancement. Weight acceptance begins with the stance period and uses the first two gait sub phases (initial contact and loading response). Single

limb support continues stance with the next two sub phases (mid stance and terminal stance). Limb advancement begins in the final phase of stance (pre-swing) and then continues through the three sub phases of the swing (initial swing, mid swing, and terminal swing) fig. (2) ***(Jacquelin, 1992).***

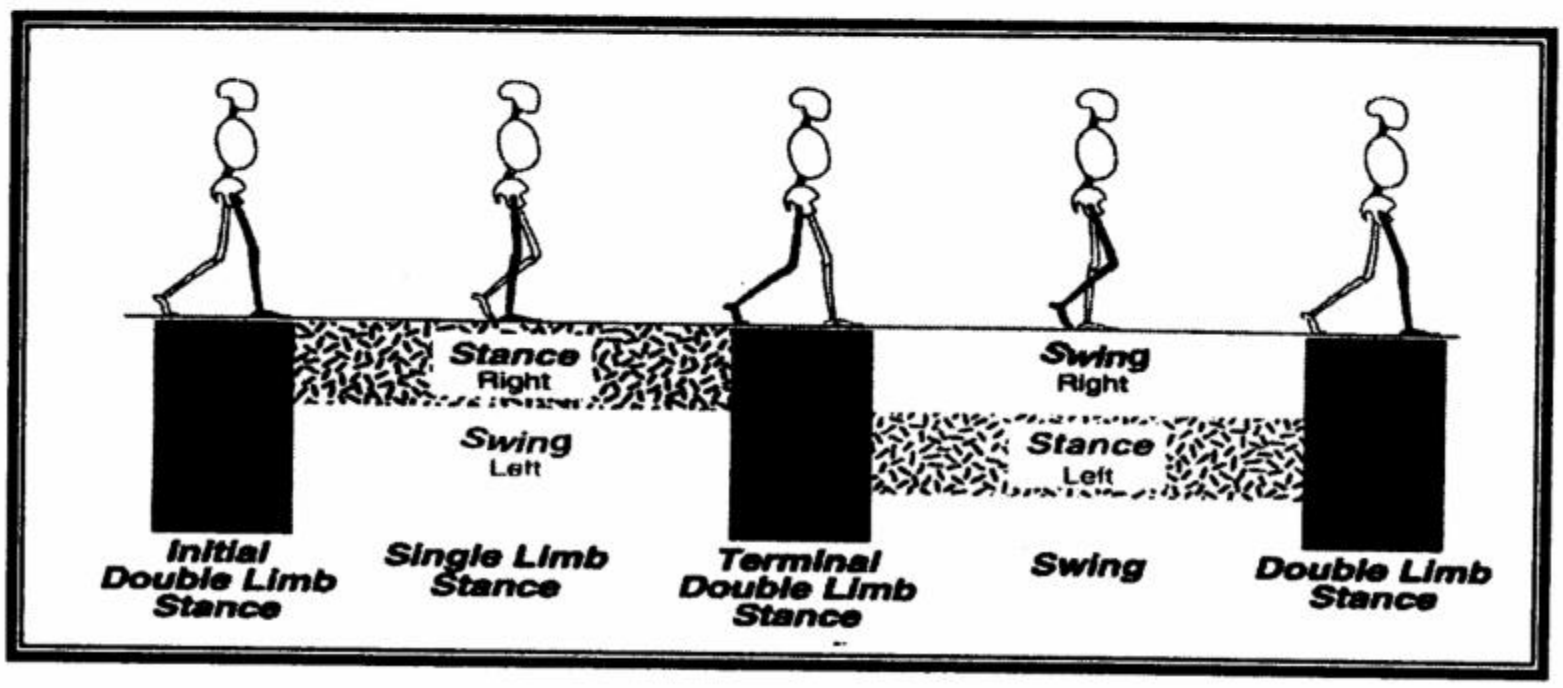

Fig. (2): Divisions of the gait cycle (Jacquelin , 1992).

Gait analysis:

Walking is a consequence of the two-way interaction between the neural networks in the central nervous system plus the intraspinal nervous system on one side and the mechanical periphery consisting of bones and muscles on the other. The muscles receive commands from the nervous system, and send back sensory information that modifies the activity of the central neurons. The coupling of these two networks produces a complex stride interval time series that is characterized by particular symmetries ***(Nicola et al., 2009).***

Before gait analysis and re-training, a thorough evaluation must be performed by the physical therapist to examine factors such as ROM,

posture, bony alignment, strength, motor control, coordination, sensation, and balance. Keeping in mind any deficits in these areas, the therapist is then ready to observe and analyze gait and speculate on which of the deficits may be contributing to a specific gait deviation. Awareness of specific problem areas allows the therapist to address these issues with key treatment strategies and modalities ***(Hayes, 1998).***

Gait analysis is the objective documentation of gait ***(Ounpuu, 1995).*** Gait analysis ranges in complexity from observational assessment to three-dimensional (3-D) motion analysis and can include tools such as videotaping, dynamic electromyographs (EMG), and force plates ***(Hayes, 1998).***

Quantitative gait evaluation:

Quantitative gait analysis system includes measurement of three primary components: kinematic, kinetics, and muscle activity. And other components such as foot switches and oxygen consumption monitoring to measure overall energy expenditure. To measure these various components, a variety of equipments are used including. 1-) optomotion analysis systems to measure kinematics, 2-) force plates to measure kinetics, and 3-) multi-channel dynamic EMG apparatus to measure electrical muscle activity in muscles during gait ***(Kerrigan et al., 1998).***

Systems used for evaluation of temporal parameters of gait:

Common temporal parameters such as velocity, cadence, and stride time can be measured to monitor a patient's progress outside of a

sophisticated gait laboratory. Velocity can be measured simply with a stopwatch as a patient traverses a designated distance. Cadence can be measured calculating the number of steps per minutes (through dividing number of steps in a designated distance on time) ***(Turnbull and Wall, 1985; Hausdorff et al., 1995).***

Computerized stride analyzers may provide the same information in a more automated fashion. Computerized stride analyzers usually consist of insoles with footswitches (i.e. pressure sensitive transducers), typically attached to the heel, toe, and occasionally the metatarsal region. Computerized stride analyzers are connected to data boxes worn by the patient either around the waist or the ankle. These sensors measure the duration of floor contact via opening and closing switches. After acquisition, data transfer and analysis are typically performed using a personal computer ***(Kerrigan et al., 1998).***

Systems used for evaluation of spatial parameters of gait:

Electrogoniometers.

Electrogoniometers are computerized versions of simple gonoimeters, which are commonly used in clinical practice to assess joint ROM. An electrogoniometer consists of one or more potentiometers placed between two bars with one bar is strapped to the proximal limb segment and the other is strapped to the distal limb segment. The potentiometer, which is placed over the joint, provides a varying electrical impulse, depending on the instantaneous angle between the two limb segments. This electrical impulse information is then interfaced to

degeneration. BTX-A is an effective treatment for limb dystonias but therapy outcome is often variable with relatively modest effects seen for occupational cramps ***(Cole et al., 1995).***

Hemifacial spasm (HFS) is a peripherally induced movement disorder characterized by chronic involuntary and unilateral contractions, involving lower and upper facial muscles. Primary HFS is commonly attributed to vascular loops compressing the seventh cranial nerve at its exit zone from the brainstem producing abnormal ephaptic transmission. BTX-A treatment of primary HFS resulted in response rates of 90–95% and the toxin is currently considered the treatment of choice for this condition ***(Mauriello et al., 1996).***

Tics are rapid, brief, semi-purposeful jerks usually affecting the face, head or upper body and are often part of the Gilles de la Tourette's syndrome. In patients with motor and vocal focal tics, a reduction in involuntary movement is obtained by injecting BTX-A in the involved muscle. BTX-A treatment also produces significant improvement in the premonitory sensations of patients affected by Gilles de la Tourette's syndrome ***(Kwak et al., 2000).***

Essential tremor is a common, often benign, familial movement disorder that can be improved by oral therapy using a number of drugs. It has been shown that BTX-A can reduce tremor intensity in severe cases ***(Jankovic et al., 1996).***

Palatal tremor (or myoclonus) is a rare hyperkinetic disorder, characterized by high frequency, rhythmic jerks of the soft palate and ear clicks. Two types are recognized, namely _essential palatal tremor_ and _symptomatic palatal tremor_. Ear clicks in palatal tremor can be very distressing and are caused by activity of the levator veli palatini muscle.

BTX-A injected in this muscle is effective treatment for the condition ***(Deuschl et al., 1991).***

Electric Stimulation

Rehabilitation encompasses various techniques. these techniques are used to manipulate elements of the central and peripheral nervous system. And includes neurodevelopmental techniques, proprioceptive neuromuscular facilitation, biofeedback, robot-assisted therapy, mirror therapy, constraint intensive movement therapy, and electrical stimulation ***(DeLisa, 1988).***

Electrical stimulation (ES) activates sensory-motor systems by delivering electrical charge in the form of bursts of electrical pulses (phasic activation). The characteristics of phasic activation are: frequency of pulses (f), pulse duration (T), and pulse amplitude (I); these are termed stimulation parameters. Recruitment of individual cells and summation of the effects of ES are directly related to stimulation parameters. Stimulation at low levels (low pulse amplitude, short pulse duration) activates afferent pathways, while strong stimulation activates both afferent and efferent pathways ***(Popovi´c and Sinkjær., 2000).***

Different electrical stimulation techniques in stroke:

Electrical stimulation of peripheral nerves.

Several research groups have suggested that electrical stimulation of peripheral sensory-motor systems contributes to the facilitation of voluntary movement, strengthening of atrophied muscles, and moderation of spasticity ***(Dejan et al., 2009).***

Low-TENS:

Low frequency Transcutaneous Electrical Nerve Stimulation (Low-TENS) consisted of application of bursts of eight pulses with interpulse intervals of about 600 ms (low frequency F = 1.7 Hz) to wrist extensors, elbow extensors, and shoulder abductors of the affected arm of stroke patients. 60-minute daily sessions, over a three month period, were performed with surface electrodes (5 cm × 3.5 cm, self-adhering gel). The intensity of stimulation was set at a level which resulted in visible contraction yet was within the comfort level. Three months of treatment resulted in a significant increase of motor function in the treatment group compared to controls; no decrease in pain or spasticity occurred ***(Sonde et al., 1998).***

MESH Glove:

In this technique, a flexible mesh glove made of conductive wire serves as the anode; conductive gel is used as the interface between the glove and skin. ***Peurala et al., (2002)*** applied only one cathode, placed proximal to the wrist. The frequency of stimulation is set at 50 Hz. The intensity of stimulation with the MESH glove is set to below and above sensory threshold levels. The electrical pulse is a short monophasic twin pulse. The glove is used with no intention to generate movement in three weeks, 20-minute sessions once or twice daily. The results suggest improved arm and hand sensation, normalized hand temperature, decreased swelling, decreased spasticity, and improved voluntary motor control.

Cyclic Electrical Stimulation: was evaluated in several studies. ***Chae et al., (1998)*** suggest that active repetitive exercise induced by cyclic ES enhances motor recovery in sub-acute stroke.

EMG-triggered electrical stimulation:

Francisco et al., (1998) assessed the efficacy of EMG-triggered neuromuscular stimulation in enhancing upper extremity motor recovery and functional recovery of acute stroke survivors. Patients treated by EMG-triggered stimulation exhibited significantly greater gains in Fugl-Meyer and FIM scores compared with controls.

Electrical stimulation incorporated into the task-related exercise:

Therapy that comprises exercise augmented with ES resulted in better and faster recovery compared with cyclic and EMG triggered ES. ***Hedman et al., (2007)*** presented ES for enhancing elbow extension with shoulder flexion and abduction movements and hand function. Subjects were instructed to adjust the stimulus amplitude only as high as was necessary to allow successful completion of the task.

Functional Electrical Therapy:

Functional Electrical Therapy (FET) involves the use of multi-channel electrical stimulation systems, designated neural prostheses, for therapy. Bionic Glove ***(Prochazka, et al., 1997; Kowalczewski, et al., 2007)*** is a neural prosthesis which integrates three channels for activation of finger extensors, flexors and thennar muscle group. The glove, which can be easily pulled over the hand and forearm, includes metal mesh that

makes contact with the corresponding contacts on the backside of the electrode. The stimulator integrates a transducer which estimates the wrist angle by using a Halleffect transducer. The Bionic Glove serves as an enhancer of thenodesis; that is, when the wrist is extended above the preset threshold, the activation of grasp pattern (stimulation of the finger flexors and thennar muscle group) will occur; when the wrist flexion angle is bigger than the preset threshold, the activation of extensors will begin. The use of the Bionic Glove requires that the patient have adequate wrist control.

Electrical stimulation with implanted electrodes:

The use of surface stimulation for therapy which we have described presents two problems. The first problem is that of insufficient selectivity, which is linked directly to the complexity of positioning of the electrodes for both stimulation and recording. The second problem is discomfort caused by electrical stimulation applied over the skin. Both problems can be reduced by means of appropriate implantable technology. One of the methods tested uses intramuscular percutaneous electrodes. The electrodes can be implanted by subdermal needles, and can be removed easily after treatment by gently pulling on the free ends which protrude from the body ***(Chae et al., 2001).***

Electric stimulation and spasticity:

Electrical stimulation has been widely studied for spasticity suppression, however, the results have been contradictory. The different outcomes may be related to the wide variety of stimulation parameters, application methods, and quantification measurements used. Spasticity was dramatically reduced during ES by stimulating the antagonistic

muscles of the wrist and finger flexors of hemiplegic patients ***(Alfieri, 1982).***

CHEN1 et al., (2005) concluded that Electrical stimulation (ES) has been used in a variety of ways to suppress spasticity. In the literature, therapeutic ES for spasticity was based on mechanisms of

A- Facilitating Renshaw cell recurrent inhibition.

B- Antagonist reciprocal inhibition.

C- Cutaneous sensory habituation.

D- Using ES to suppress spasticity by facilitating the autogenic Ib inhibitory.

Jane and Lois (2007) stated that electrical stimulation delivered at both sensory and motor amplitude has been reported to reduce impairment and improve arm function following stroke. Neuromuscular electrical stimulation following stroke reports improved force production, selective activation of muscles, passive range of motion, and reduction of abnormally high muscle tone. Sensory amplitude electrical stimulation has been reported to enhance sensorimotor recovery following stroke.

Therapy combining Bobath inhibitory technique and electrical stimulation may help to reduce spasticity effectively in stroke patients. Another method for reducing spasticity is neuromuscular electrical stimulation over the agonist or antagonist muscles of spastic muscle. There is some evidence that electrical stimulation of the antagonist muscles can reduce spasticity immediately following treatment. Neuromuscular electrical stimulation may increase sensory inputs into the central nervous system and so accelerate nervous plasticity and lead to faster motor learning ***(Amir and Elham, 2008).***

LINDA et al., (2005) concluded that TENS has also been found to be effective in reducing spasticity in neurological conditions such as cerebral vascular accident (CVA), spinal cord injury (SCI), and multiple sclerosis (MS).

Effect of electric muscle stimulation in enhancing botulinum toxin effect:

Electric stimulation, of various stimulation frequencies used could differentially affect the absorption of BTXA. Experiments investigating the time of appearance and amount of spontaneous EMG activity in the EDB muscles may help to explain how NS boosts the BTXA induced neuromuscular blockade ***(Emma et al., 2005).***

Direct electrical stimulation of the muscle delays sprouting. ***Black and Dolly (1986a)*** found early denervation activity in stimulated EDB muscles but no reinnervation potentials in stimulated or nonstimulated EDB muscle up to day 60 after BTXA injections.

Electric stimulation facilitate the lytic step that blocks acetylcholine transmission at the neuromuscular junction. Which enhances the effect of BTXA-induced denervation ***(Simpson, 1980).***

Chapter III

SUBJECT ,MATERIALS , AND METHODS

Chapter III

SUBJECTS, MATERIAL AND METHODS

The purpose of this study was to determine the effectiveness of electrical muscle stimulation on enhancing botulinum toxin action in spastic stroke patients. This chapter includes (1) sample selection; (2) Instrumentation; (3) Procedures; (4) Data collection and (5) Statistical analysis

Sample selection:

Forty adult stroke patients of both sexes (20 males and 20 females) ranging in age from 45 to 55 years were included in the current study. The patients were selected from Faculty of physical therapy outpatient clinic. Selection of the patients was based on careful history taking and clinical examination **(appendixIII).** The diagnosis was confirmed by CT or MRI of the brain. Stroke diagnosis was made by the treating physician according to the WHO definition of stroke "to exclude TIAs". All subjects were provided with information sheet and signed consent form **(appendix IV).**

Inclusion criteria (appendix VI):

- Patients age ranged from 45 to 55 years.
- Duration of illness ranged from six to eighteen months.
- Degree of spasticity ranged from two to three according to modified Ashworth's scale ***(Bohannon and Smith, 1987).***
- Patients were able to walk independently.

- None of the patients received Botulinum toxin injection before the study.

- The patients were medically stable with no hospitalizations for the previous two months.

- The patients have sufficient cognition that enables them to understand the requirements of the study.

Exclusion criteria:

- Patients with any other neurological deficits such as root compression.

- Patients with any orthopedic abnormalities such as contracture or deformity affecting lower limbs or gait.

- Patients with impairment of sensation.

- Patient with Cardiopulmonary disease which decreases the patient tolerance and activates.

The patients were divided randomly into two equal groups, the study group (G1) (n=20) received the botulinum toxin injection in the calf muscle plus selected physiotherapy treatment program and electric muscle stimulation. While the control group (G2) (n=20) received botulinum toxin injection in the calf muscle plus selected physiotherapy program and placebo electric muscle stimulation.

Instrumentation:

For assessment:

The pro-reflex system.

It is the system that is used to evaluate gait parameters and included the Q-Trac Software which consists of camera system with three

cameras (fig.4), reflective dots (fig.5), a wand–Kit used for calibration of the system (fig.6), and eight meters long walkway (fig.7). A PC with installed Q Trac software. Made in Sweden.

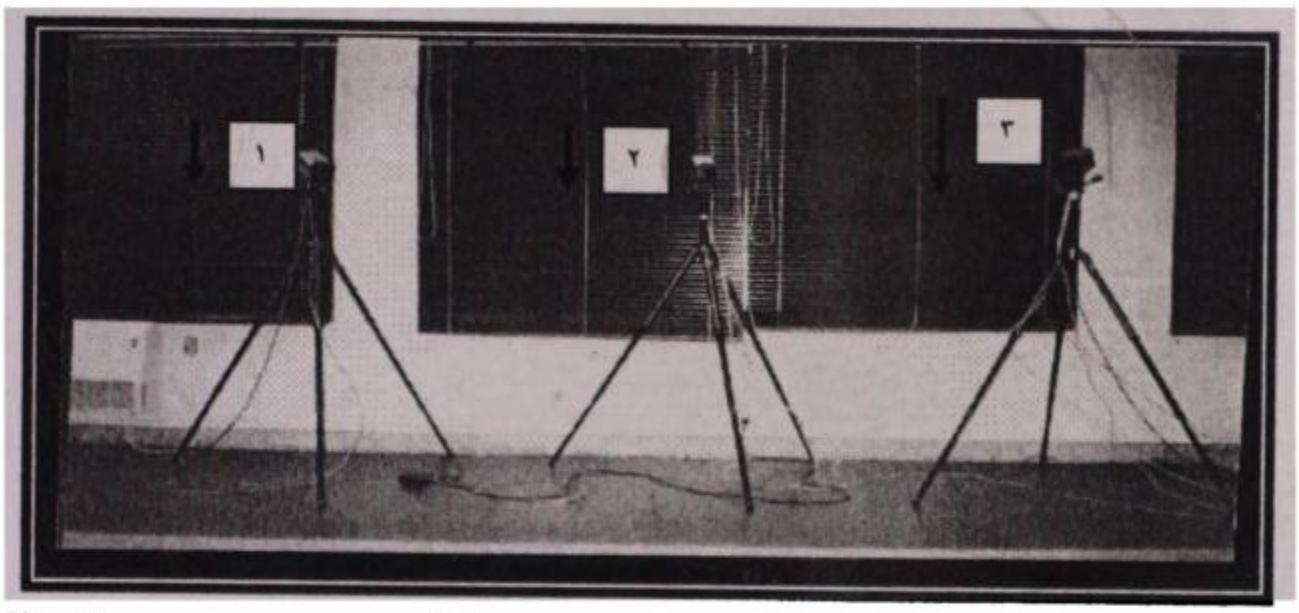

Fig. (4): Camera system, (three cameras, 1,2,3) (Motion analysis lab, Faculty of Physical Therapy, Cairo University).

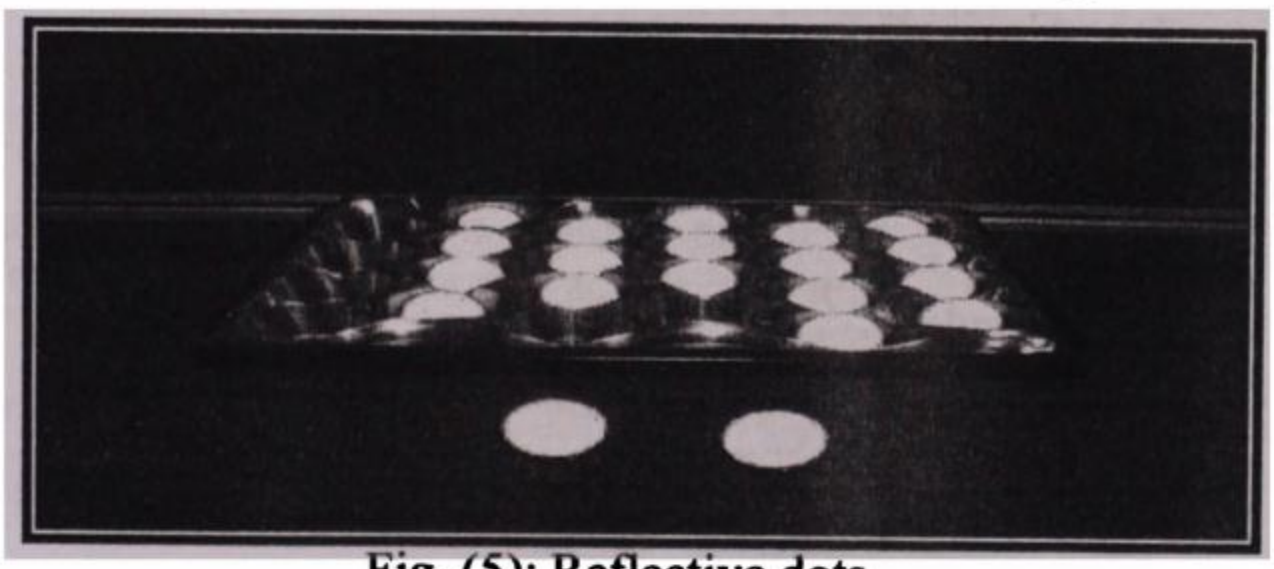

Fig. (5): Reflective dots

(Motion analysis lab, Faculty of Physical Therapy, Cairo University).

Fig. (6): The Wand-Kit (Motion analysis lab, Faculty of Physical Therapy, Cairo University).

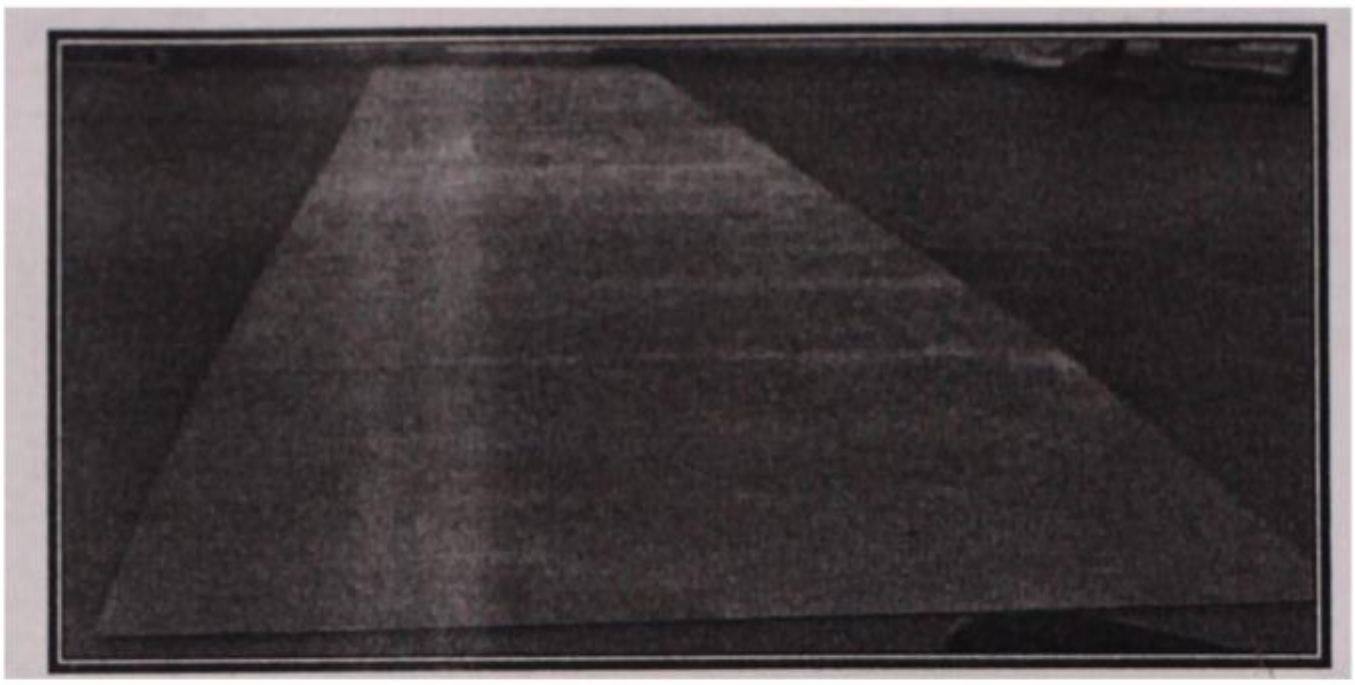

Fig. (7): Eight meters walk-way (Motion analysis lab, Faculty of Physical Therapy, Cairo University).

Electromyography:

The device components are:

A- Stimulating Unit: to which the stimulating electrode was connected.

B- Amplifiers: four electrically isolated amplifier channels with impedance less than 100m ohm and sensitivity up to 4000V/0.5. The amplifier gains up to 10 traces on the screen with resolution of 1000 points per trace which were available.

C- Electrodes: ground electrode, bipolar stimulating electrode with inter electrode distance of 2.5cm and two silver surface recording electrodes (one is active and the others is the reference).

Before the apparatus was used for calculating H/M ratio, the commit company calibrated all tested parameters for more accuracy and objectivity. fig. (8).

Fig. (8): Electromyograghy :Neuroscreen plus version 1.59 produced by Tonneis a division of Erich Jseger Gmbh, Germany: 1998, was used in current study.

For treatment:

The used apparatus is phyaction787 made in Netherlands, serial number 27598nm carry frequency 2500HZ with modulated frequency 20Hz (bipolar current) in faculty of physical therapy fig. (9).

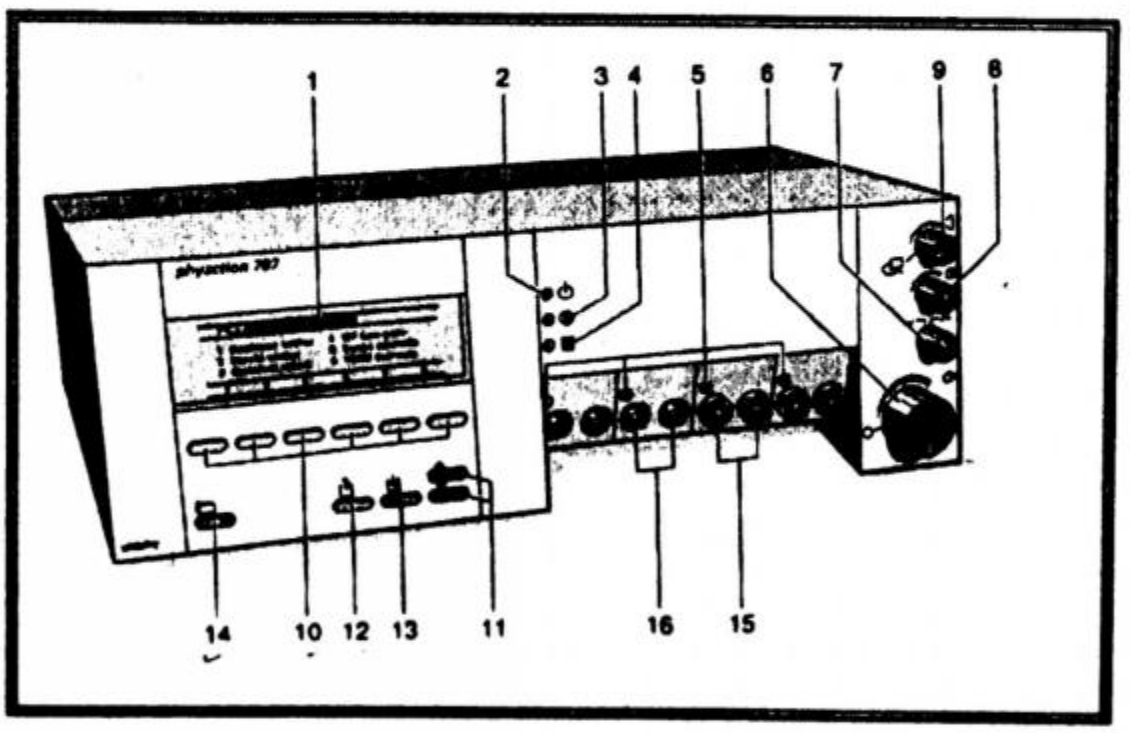

Fig. (9): Electric muscle stimulator.

Procedures:

Evaluation Procedures:

Evaluation environment was constant through the study. The evaluation procedures were done by the same physiotherapist. A detailed clinical and neurological sheet was done to all patients Appendix (V).

Patient orientation: a brief explanation about the protocol of evaluation was given to each patient. The evaluation procedures done initially and repeated after one and six weeks of treatment, including;

Evaluation of gait:

Using the pro-reflex system in the following steps.

(1) Setup: This step included three main points:

1-Setting up the patient:

The patient was asked to take off his/her cloths to expose both lower limbs up to thighs. The reflective dots were placed on the selected bony landmarks by sticky material (at hip, knee, ankle and toes) (fig.10).

Hip dot: over greater trochanter.

Knee dots: are placed on the middle of the lateral knee joint line, supra pattelar and tibial tuberosity.

Ankle dots: are placed on the lateral malleolus, 30 millimeters proximally from the lateral malleolus and over the lower end of tendoachilles just above calcaneous.

Toe dot: it is placed on the foot between the second and third metatarsals, 10-15 millimeters proximal to the metatarsal heads.

Each patient was asked to stand at the border of the measurement area, where the dots were visible in the cameras. Then the patient was asked to walk and at the middle of the selected measurement area, he or she was captured. The walking was repeated three times and the mean value of gait parameters was calculated.

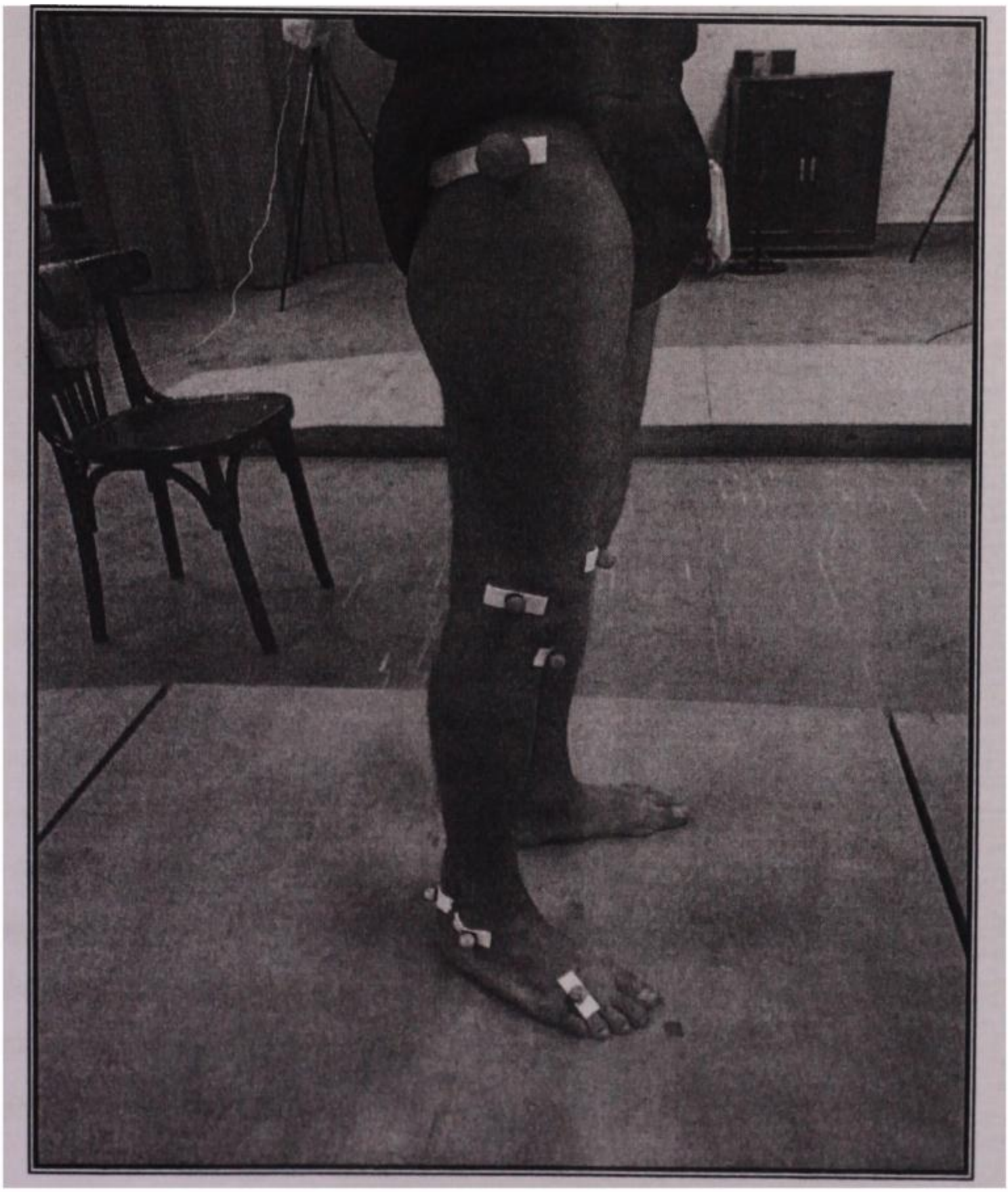

Fig. (10): Placement of the skin dots.
(hip, knee, ankle and toe dots)

2-Camera Placement:

The three cameras which were used in capturing the patient motion were arranged on one side of the eight meters long walkway at a height of 1.5 to 2 meters. The patient stood midway on the walkway, to ensure that all cameras view the patient (fig.11).

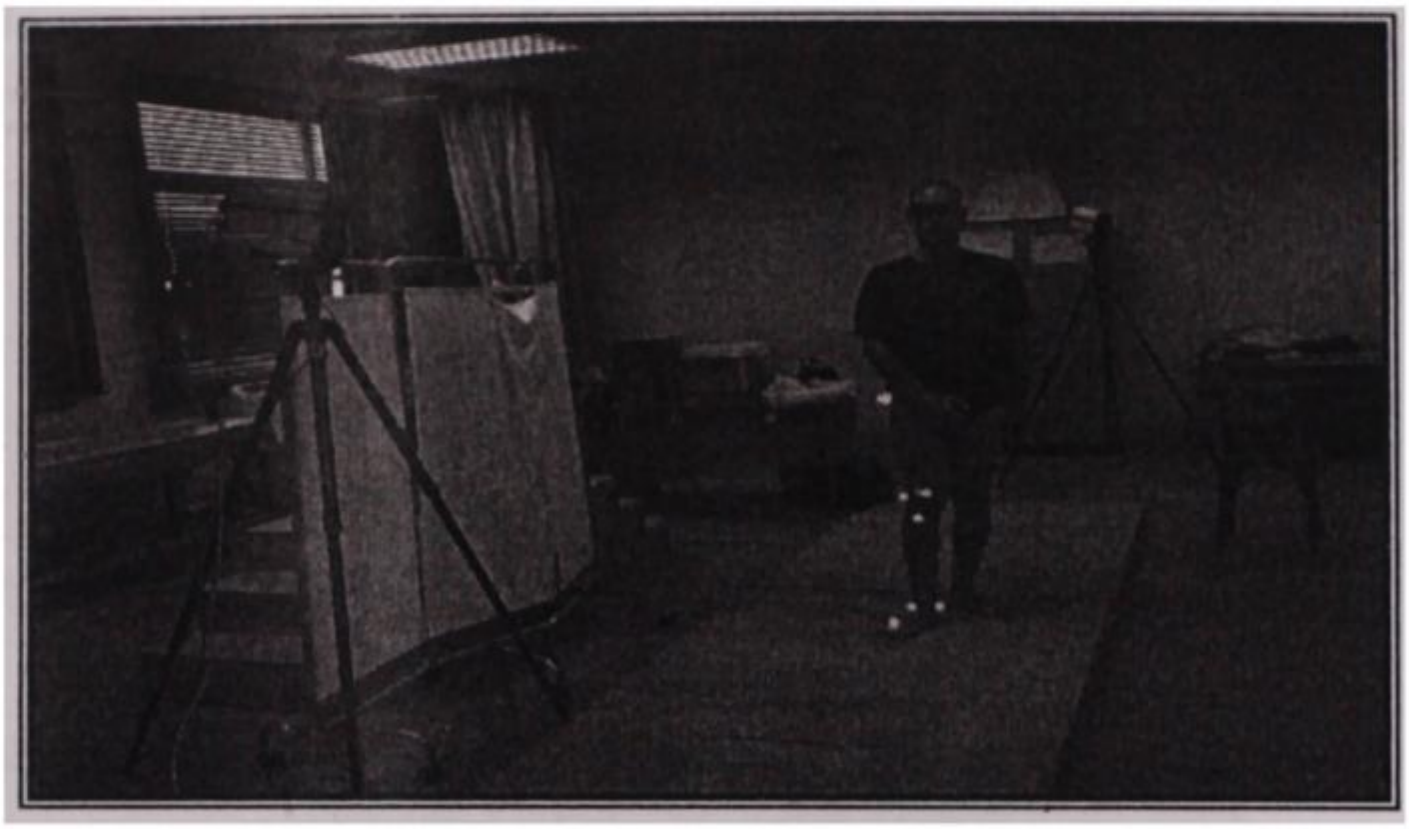

Fig. (11): Capturing the patient motion.

3-Measurement area:

The measurement area was the part on the walkway that the patient would walk along. It is about three meters that required performing three complete gait cycles. Primarily, the measurement area was marked on the wooden walkway by placing four reflected dots at the four corners of the selected distance of the walkway, which had to be visible in the cameras during the setup (fig.12).

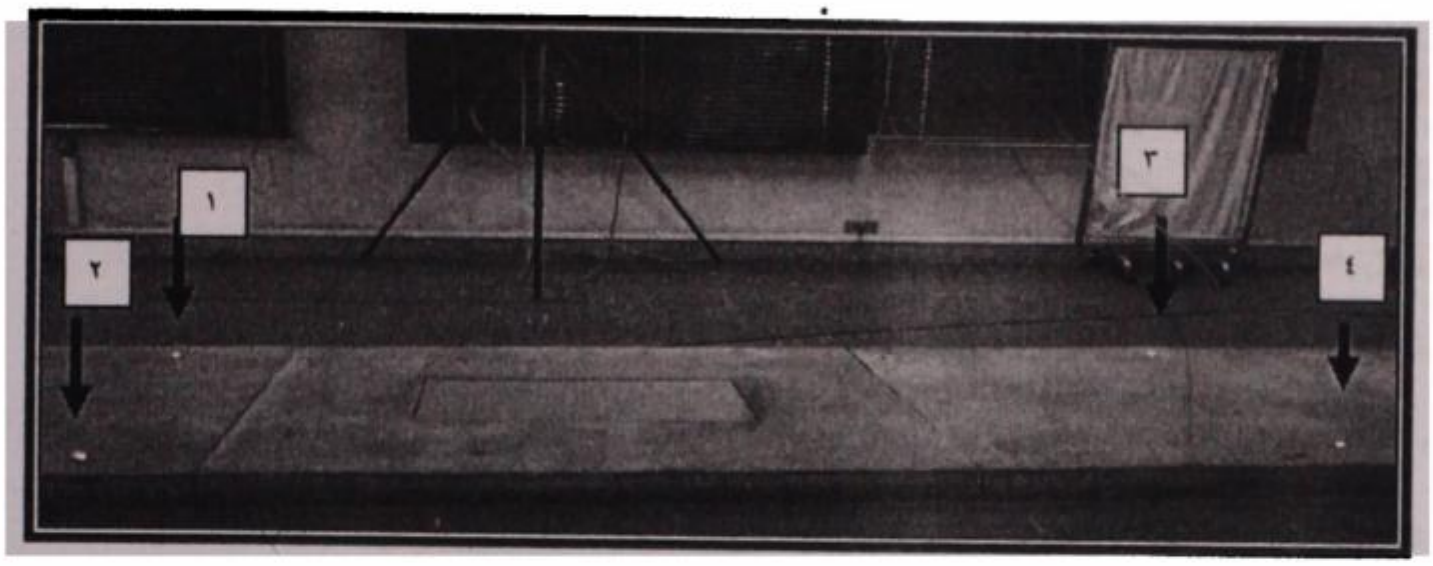

Fig. (12): Measurement area, the arrows identify the start and the end of the measurement area. -1 and 2 are the start of the measurement area.

-3 and 4 are the end of the measurement area.

(2) The pro-reflex system Calibration:

Before any three-dimensional (3-D) capture performance, the camera system was calibrated to assure accuracy of the obtained values. This calibration required these tools: A wand to provide the camera system with the measurement points to be used for the calibration. A reference structure for defining the calibration coordinate system. The reference structure was placed horizontally along the floor in the measurement area which is covered by the cameras. All cameras viewed the four markers of the structure. Once all parameters are correctly set up, the calibration will be performed by pressing the capture button and moving the wand around in the measurement volume during the calibration data retrieval. During the calibration capture, the wand should be positioned in the three dimensions, starting with Z, X then Y directions respectively (fig. 13 a, b, c).

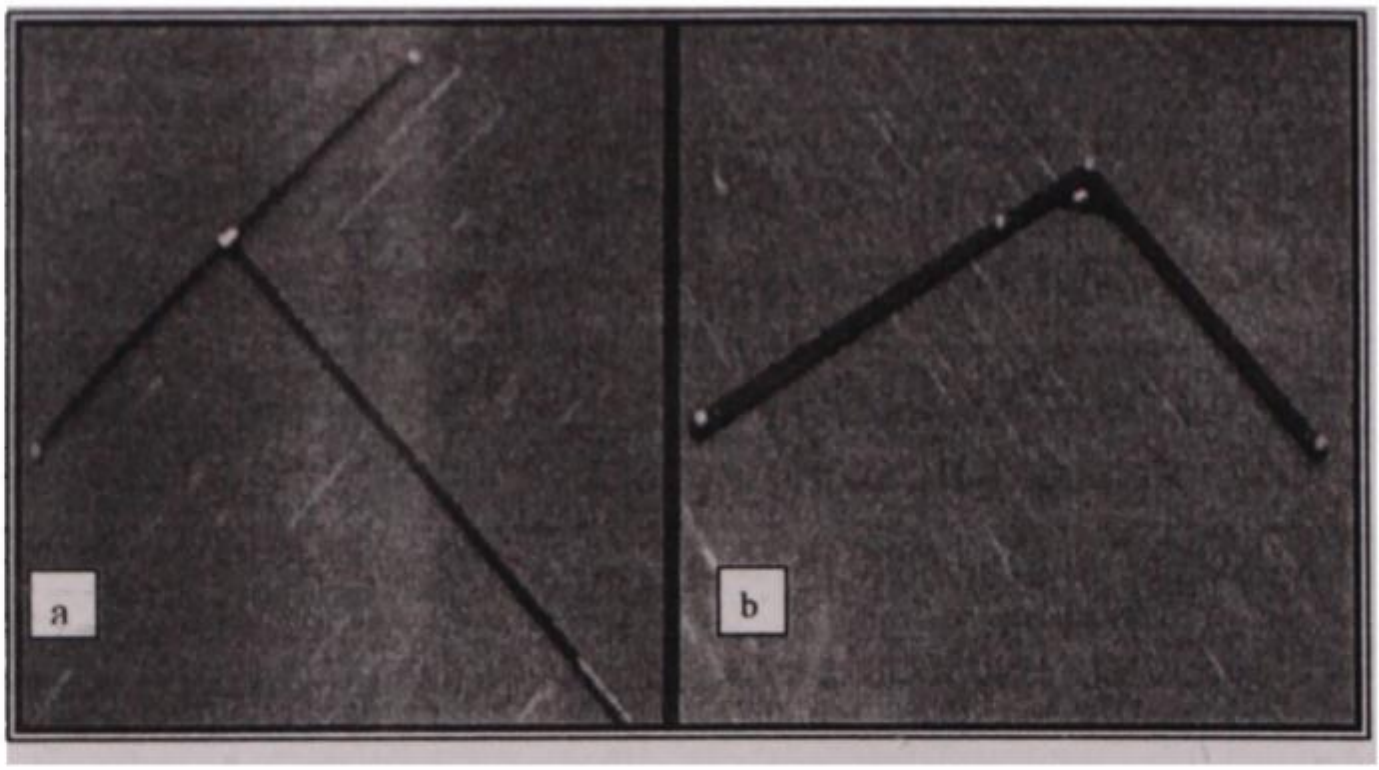

Fig.(13 a, b):(a)The wand for calibration, (b) The reference structure.

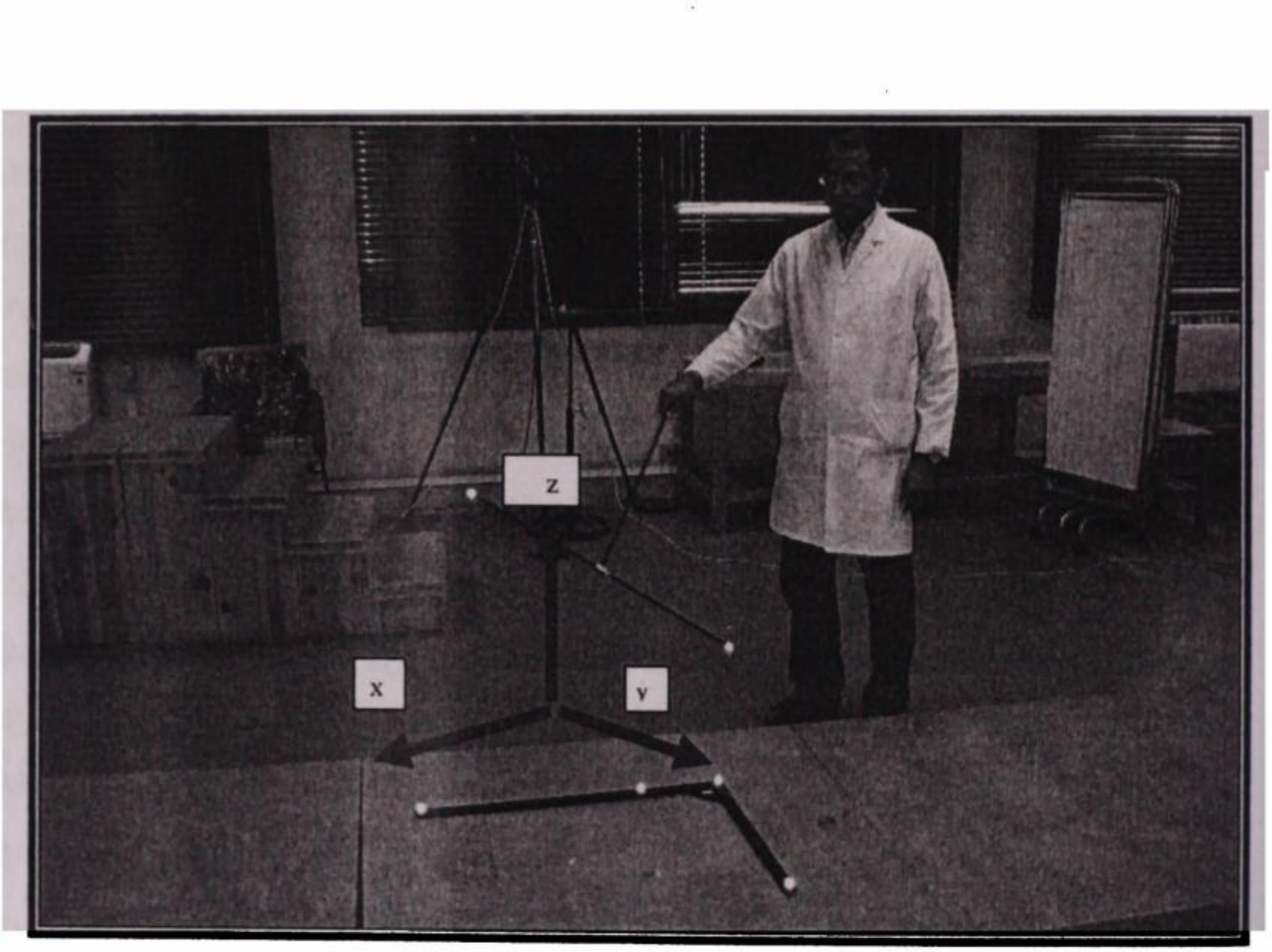

Fig. (13, c): Calibration process, the wand was positioned in all three dimensions (X, Y, Z).

(3) The pro-reflex system Capture:

A new file was opened for each patient including subject data (name, age, weight, height). The patient was asked to start walking from the starting point which was determined previously. When the patient passed the measurement starting position, the Q Trac measurement was be started. The patient was instructed to continue walking to the end of the walk way until the Q Trac measurement is completed. The capture was initiated by selecting capture from the menu bar and the measurement should be saved. Three trials were performed for each patient and the mean values were calculated fig. (14).

Fig. (14): Tracking the patient motion (Capture three complete gait cycles).

(4) The pro-reflex system Export:

It is the transfer of the selected gait cycles to the tabulated separated values (TSV) file for analysis. Data Processing included two main steps (1) Tracking of motion of the patient and names the skin dots each by its position on each landmark, (2) Selection of three complete gait cycles and export of this selection to the analysis file.

(5) The pro-reflex system Analysis:

Dots used for the calculations were then identified. Finally the calculations were initiated with the Run button. When the calculation were completed, the results were displayed showing the calculated global gait parameters in tables and figures.

H/M ratio measurement:

All the patients were subjected to measure the H/M ratio. This measurement was measured from triceps soleus muscle. The sites of stimulating and recording electrodes were cleaned by rubbing the skin using alcohol. The procedure was repeated until the skin became slightly red to ensure removing of the degenerated cell and lowering the skin resistance. Precautions were taken to avoid irritation especially at the stimulating site. Before running the test, the whole procedure was explained to the patients.

Electrodes placement:

During recording, care was taken no interruption and the room was quiet to avoid any changes in the reflex value. The patient was placed in prone position comfortably on the examining table. The head of the patient was held in mid position to avoid alteration or distribution of tone over the patient's body during recording. The feet were placed over the edge of the table with a pillow placed under the ankle, so that the ankles were placed in a relaxed position. Recording was conducted from the soleus muscle as follows: fig. (15).

a. The active (negative) electrode was placed along the mid-dorsal line of the lower leg, 2cm below the point of separation of the gasterocnemius and secured by adhesive plaster.

b. The other indifferent (positive) electrode was placed distal to the active electrode in a straight line and secured by adhesive plaster.

c. The ground electrode was placed between the stimulating and recording electrode.

d. The stimulating electrode was placed over the tibial nerve just medial to the midpoint of the knee crease in the popliteal fossa.

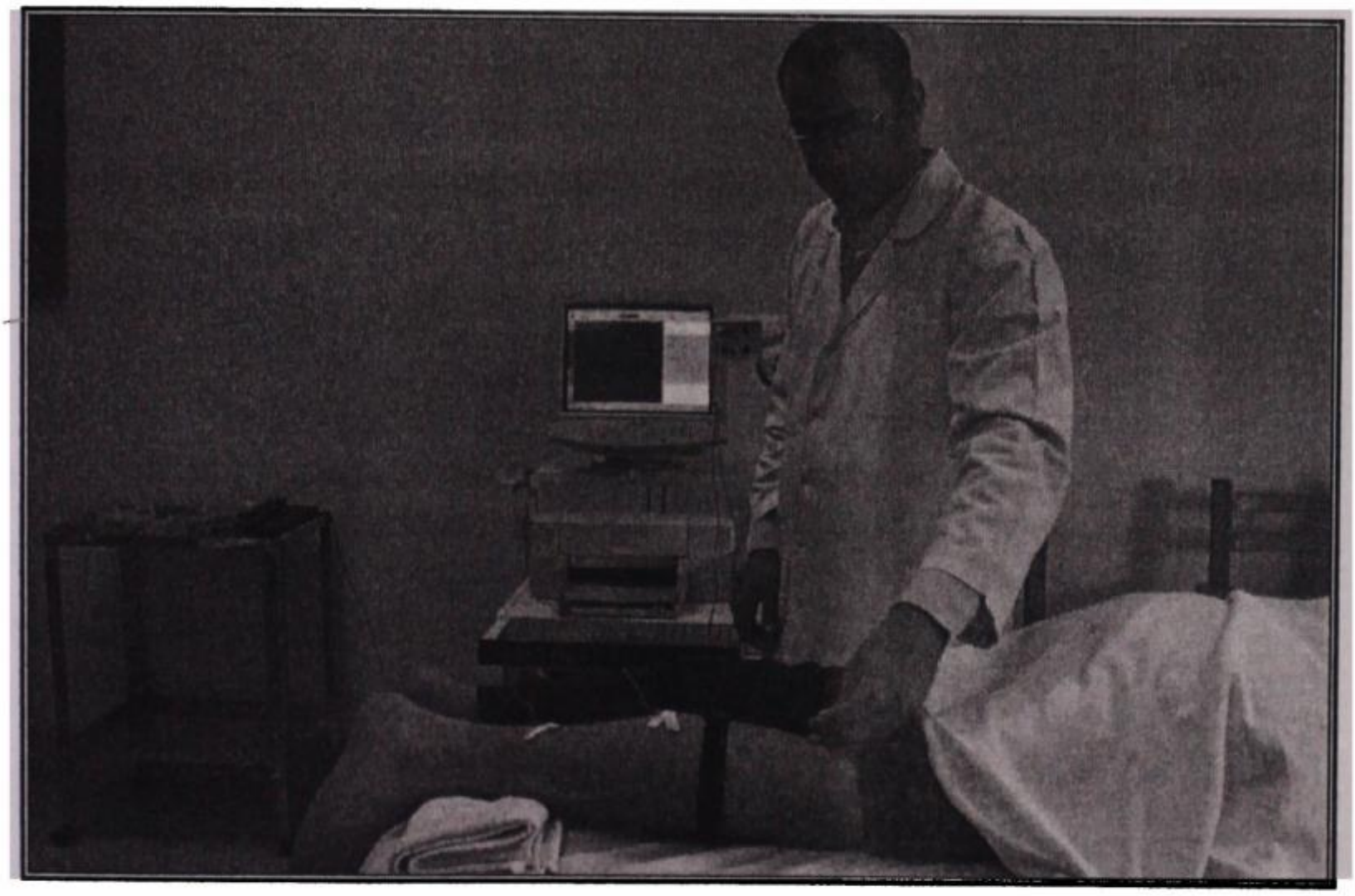

Fig. (15): measuring H/M ratio.

The stimulation duration was 1msec, which makes it more selective for stimulating the afferent Ia nerve fibers and evokes a stable H-reflex. Stimulation was at rate of once every three seconds to avoid blocking response and allow full recording of the reflex response. After adequately fitting the different electrodes in the previously described

Chapter V

DISCUSSION

The current study was conducted to explore the effect of using electric muscle stimulation in enhancing botulinum toxin action in spastic stroke patients. Forty female and male stroke patients were included. The patients assigned randomly into two equal groups. The study group received Botulinum toxin-A injection in the calf muscles plus selected physical therapy program three sessions per week for six weeks plus electric muscle stimulation, daily for seven days post injection. The control group received Botulinum toxin-A injection in the calf muscles plus selected physical therapy program three sessions per week for six weeks plus placebo electric muscle stimulation daily for seven days post injection.

Functional and laboratory (walking velocity, H/M ratio and ankle joint angle at initial contact) assessment for spasticity and gait were performed before intervention and were repeated after one week and six weeks of treatment. In this study, the degree of spasticity was assessed using H/M ratio depending on ***Little and Halar, (1985).*** Who stated that the H/M ratio has been used to assess the excitability of the motor nucleus by determining the percentage of motor neurons activated via the H-reflex in comparison to direct activation of the motor neurons. There is increase in H/M ratio in the spastic phase of hemiplegia and spinal cord injuries.

The rationale of selection of walking velocity to assess improvement was that the temporal aspects of hemiplegic gait are characterized by reduced walking velocity and increased cycle time ***(Brandstater et al., 1983; Chen et al., 2005 and Lin et al., 2006).***

The rationale of selection of ankle joint angle at initial contact as an indirect measurement of spasticity. This selection is based on the fact that the primary cause of gait asymmetry in stroke patients is planterflexion spasticity ***(Tang and Jan, 2003).***

Initially the pre treatment data shows that stroke patients have increase in their H/M ratio which ranged from 1.9 to 4.4 *mV*. ***Levin and Chan, (1993)*** found that the H/M ratio is a reliable indication of spasticity and can be used to assess the effects of treatment intervention repeated over days and weeks.

Stroke patients have increase in the ankle joint angles in planterflexion at initial contact, and decrease in their walking velocity. Normal angle at initial contact is either in neutral position or planterflexion 3°-5° degrees ***(Jacquelin, 1992).*** Patients in this study had their ankle joint angles at initial contact ranged from 17.00° to 32.00° degrees, and walking velocity ranged from 0.20 to 0.46 m/s. This indicates that the pre treatment values of ankle joint angles at initial contact and walking velocity in those patients were far from normal values. This agrees with ***O'Sullivan and schmtiz, (1994)*** and ***Higginson et al., (2006)*** findings who stated that during the stance phase of the hemiparetic leg, the patient may exhibit foot flat or even a "forefoot first " at the initial contact instead of a heel strike with inadequate ankle dorsiflexion. ***Chen et al., (2005) and Lin et al., (2006)*** stated that hemiplegic gait are characterized by reduced walking velocity and increased cycle time.

In this study there was great decrease of spasticity in both groups as the H/M ratio drops significantly in comparing the pre treatment data to post treatment one results (results after one week), and post treatment

two results (results after six weeks). This indicates that both treatments are effective after one and six weeks.

These findings come in accordance with the results of **Dolly et al., (1982)** who found that BTX-A EMG guided intramuscular injection causes temporary reversible blockade of acetylcholine release at the neuromuscular junction that leads to temporary muscle weakness. Logically, this controlled weakness will reduce the available force of involuntary contraction as well as unwanted cocontraction. This paralytic effect usually lasts for three–four months. It is the basis for the clinical benefit of BTX-A treatment, which can persist for up to six months.

Also there was a significant difference in comparing H/M ratio in study to control groups in post treatment one and post treatment two results, which indicates adding electric muscle stimulation after BTX-A injection have the superior results. These findings come in accordance with the results found by **Simpson, (1980)** who stated that electric stimulation facilitates the effect of BTX-A induced denervation. Direct electrical stimulation of the muscle delays sprouting **(Black and Dolly 1986a).** Electric stimulation, of various stimulation frequencies could affect the absorption of BTX-A **(Emma et al., 2005).**

In this study there was no improvement in walking velocity in both groups in comparing the pre treatment data to post treatment one results (results after one week). But there was improvement in comparing the pre treatment and post treatment two results (results after six weeks). This indicates that both treatments are effective after six weeks.

These findings come in accordance with the results found by **Hamjian and Walker, (1994)** who stated that functionally, spastic cocontraction is a major factor impeding active movements. Injection of BTX-A into an overactive muscle may reduce its spastic cocontraction and improve movement. The main goals of BTX-A treatment of muscles of the leg and foot are improvement in active function and increased participation, improved walking velocity and quality, and reduced reliance on walking aids.

Spastic cocontraction is defined during volitional command to an agonist, by the inappropriate recruitment of the antagonist muscle sensitive to its degree of stretch **(Gracies, 2001).**

There was a non significant difference in walking velocity in comparing study to control groups in post treatment one but in comparing study to control groups in post treatment two results there was a significant difference. This indicates adding electric muscle stimulation after BTX-A injection have the superior results after six weeks.

These findings come in accordance with the results found by **Eleopra et al.,(1997; Rodriquez et al., (2000); Hesse et al., (2002); and Ward et al., (2003)** the author stated that there are various rehabilitative techniques to increase BTX-A internalization and diffusion. Such as serial casting, stretching, functional electrical stimulation, occupational therapy and therapeutic exercise.

In this study there was improvement only in study group in ankle joint angle at initial contact in comparing the pre treatment data to post treatment one results (results after one week). This indicates that treatment in study group was effective after one week. Also there was

improvement in both groups in comparing the pre treatment and post treatment two results (results after six weeks). This indicates that both treatments are effective after six weeks.

These findings come in accordance with the results found by **Emma et al., (2005)** who suggest that NS increases BTX-A induced paresis. Therapy with BTX-A and NS combined could accelerate the toxin's action on muscles and allow a more rapid and persisting improvement in a spastic posture. It could also help to reduce the dose of this expensive drug and favorably alter the balance between the benefits and side effects of this type of therapy.

Also there was no significant difference in comparing ankle joint angle at initial contact values of study to control groups in post treatment one. But in comparing ankle joint angle at initial contact values of study to control groups in post treatment two results there was significant difference. This indicates adding electric muscle stimulation after BTX-A injection have the superior results after six weeks.

These findings come in accordance with the results found by **Eleopra et al., (1997)** who studied the effect of electric stimulation in normal EDB muscle injected with BTX-A, and found that low-frequency stimulation induces a larger CMAP decrement in the stimulated than in the non stimulated EDB. **Hesse et al., (2001)** stated that in spastic muscles, high-frequency stimulation of injected muscles significantly improves elbow spasticity in hemiparetic patients treated with BTX-A and electrical stimulation of the upper limb.

In this study there was a strong positive correlation between H/M ratio (degree of spasticity) and ankle joint angle at initial contact values, in both groups in all measurements. Also there was a strong negative correlation between H/M ratio (degree of spasticity) and walking velocity

values, in both groups in all measurements. Also there was a strong negative correlation between ankle joint angle at initial contact and walking velocity values, in both groups in all measurements.

The last facts come in accordance with **Jorgensen et al., (1995) and Gaviria et al. (1996)** who stated that the major factors affecting stride length and walking velocity were the severity of motor involvement and the degree of leg paresis. **Higginson et al., (2006)** stated that the patient may exhibit both planterflexion and inversion at initial contact and then begin to bear weight on the lateral border of the foot, as a result of over activities of tibialis anterior and premature activation of the planter flexors.

By reviewing the last data we could reach to the fact that:

Muscle over activity is not evenly distributed throughout the body. Across joints there is frequently imbalance between agonist and antagonist, producing abnormal joint postures and movement patterns. Due to the asymmetric nature of the abnormal activity, local rather than systemic treatment is recommended. Because of the biomechanical link between gait dysfunction and muscle overactivity, many investigators have tested the effect of BTX-A injection to improve walking. Plantarflexor spasticity causes a number of problems during walking. These include: initial contact with forefoot rather than heel, reduced loading and stance duration on the affected limb, stance equinus, reduced stride length impeding progress, lack of push-off, and dragging of the toes ***Gracies et al., (2002).***

The treatment of muscle spasticity is usually undertaken as part of a holistic rehabilitation programme that seeks to reduce the subject's disability and to promote their social participation (that is, reduce handicap). Under these circumstances the overall rehabilitation care is

likely to be more important in producing functional change than a single specific intervention, such as BTX-A injections.

It is important to recognize that BTX-A should be used as an adjunct rather than alternative to a combination of physical treatments. It is usually inappropriate to use this intervention outside of a combination of physical treatments. Careful assessment of all of the factors contributing to disability and the development of a comprehensive, preferably multi-disciplinary, treatment plan will optimize patient outcomes. It is suggested that muscle inactivity may delay this activation process of BTX-A, while ES influences the toxin uptake and onset latency. Many investigators demonstrated that repetitive ES of the axon increased BTX-A absorption **(Emma et al, 2005)**. To enhance the effects of BTX-A, some authors have hypothesized that there could be different ways to increase its internalization and diffusion. Hence, various rehabilitative techniques have been utilized, such as serial casting, stretching, functional electrical stimulation, occupational therapy and therapeutic exercise. The effect of treatment with botulinum toxin diminished with time and muscle tone had increased in the patients involved in this study. However, despite this increase in muscle tone, the improvement in the trajectory of the affected foot was sustained. Walking velocity remained high, even in the presence of hypertonicity ***(Hesse et al., 1998, and Stefano and Molteni; 2005).***

In this study; the treatment had positive effects on ankle, showing an improvement of ankle joint angle at initial contact. This is representative of a better mechanical position of lower limbs for weight acceptance. walking velocity improved. BTX-A treatment reduces the dominance of the ankle plantarflexors over the antagonist muscles, and

tibialis anterior was not contrasted by the abnormal gastrocnemius activity any more.

These facts come in accordance with the results found by **Chen et al., (1999), Bayram et al., (2006)** who stated that in hemiparetic patients an augmentative effect of periodic electrical stimulation during the three days after BTX-A injection. Moreover, these facts come in accordance with the results found by **Giovannelli et al., (2007)** who stated that Botulinum toxin type A is rarely a treatment in isolation; in clinical practice it is often given in combination with physiotherapy to obtain the maximum benefit.

In conclusion, this study suggests that electric muscle stimulation increases BTX-A induced paresis. Therapy with BTX-A and electric muscle stimulation combined could accelerate the toxin's action on muscles and allow a more rapid and persisting improvement in a spastic posture. It could also help to reduce the dose of this expensive drug and favorably alter the balance between the benefits and side effects of this type of therapy.

Chapter VI

SUMMARY , CONCLUSIONS AND RECOMMENDATION

CHAPTER VI
SUMMARY, CONCLUSION AND RECOMMENDATIONS

This study was conducted to evaluate the effect of electric muscle stimulation in enhancing botulinum toxin action in spastic stroke patients.

Forty adult stroke patients were included. The onset of the disease ranged from six to eighteen months. The patients were 20 females and 20males ranged in age from 45 to 55 years. The patients were assigned randomly into two equal groups. The study group (n = 20) received Botulinum toxin-A injection in calf muscles plus selected physical therapy program three sessions per week for six weeks plus electric muscle stimulation, daily for seven days post injection. Whereas control group (n = 20) received Botulinum toxin-A injection in calf muscles plus selected physical therapy program three sessions per week for six weeks plus placebo electric muscle stimulation, daily for seven days post injection. Each patient of the two groups was evaluated before and after one week and six weeks of treatment and the collected data was statistically analyzed using t-test.

Comparison between study and control groups revealed a significant difference regarding the H/M ratio, walking velocity and ankle joint angles at initial contact. These results revealed that electric muscle stimulation with the used parameters in this study can increase the effect of botulinum toxin A in decreasing spasticity and in improving gait in spastic stroke patients.

Conclusion

On the basis of the present data, it is possible to conclude that electric muscle stimulation with the used parameters in this study can increase the effect of botulinum toxin A in decreasing spasticity and in improving speed of gait in spastic stroke patients.

Recommendations

The results of the present study offered the need for considering the following recommendations:

- It is recommended to use electric stimulation with the used parameters in this study to improve BTX-A action in decreasing spasticity in spastic stroke patients.
- Another research should be applied in controlling the spasticity on other muscles in the lower limbs.
- Further study is needed to explore the effect of electric muscle stimulation in enhancing botulinum toxin action on upper limbs.
- Further investigations are needed to evaluate the influence of botulinum toxin on pain.
- Other studies are needed with other neurological conditions such as multiple sclerosis patient who suffering from spasticity.
- Other studies are needed with spastic CP children.